| CACC                  | TCTA | AGC 1 | CGG | AGCGC | GC GT | CTAC | ecec | Gli |            | Glu | C AAC<br>C Asn | 54  |
|-----------------------|------|-------|-----|-------|-------|------|------|-----|------------|-----|----------------|-----|
| GGC 1                 |      |       |     |       |       |      |      |     |            |     |                | 102 |
| Pro C                 |      |       |     |       |       |      |      |     |            |     |                | 150 |
| CGC (                 |      |       |     |       |       |      |      |     |            |     |                | 198 |
| GGC (                 |      |       |     |       |       |      |      |     |            |     |                | 246 |
| ACC Thr               |      |       |     |       |       |      |      |     |            |     |                | 294 |
| ATC I                 |      |       |     |       |       |      |      |     |            |     |                | 342 |
| CTC C<br>Leu 1<br>105 |      |       |     |       |       |      |      |     |            |     |                | 390 |
| TTT (                 |      |       |     |       |       |      |      |     |            |     |                | 438 |
| TTC ?                 |      |       |     |       |       |      |      |     | CTT<br>Leu |     |                | 486 |
| CTG (                 |      |       |     |       |       |      |      |     |            |     |                | 534 |
| GAC (                 |      |       |     |       |       |      |      |     |            |     |                | 582 |

#### Figure 1 (cont'd.)

|      |      | ACG<br>Thr<br>190 |      |      |      |      |      | 630  |
|------|------|-------------------|------|------|------|------|------|------|
|      |      | AAT<br>Asn        |      |      |      |      |      | 678  |
|      |      | AAC<br>Asn        |      |      |      |      |      | 726  |
|      |      | Lys<br>Lys        |      |      |      |      |      | 774  |
|      |      | CTC<br>Leu        |      |      |      |      |      | 822  |
|      |      | CCT<br>Pro<br>270 |      |      |      |      |      | 870  |
|      |      | GAC<br>Asp        |      |      |      |      |      | 918  |
|      |      | ATA<br>Ile        |      |      |      |      |      | 966  |
|      |      | TTT<br>Phe        |      |      |      |      |      | 1014 |
| <br> | <br> | <br>GCC<br>Ala    | <br> | <br> | <br> | <br> | <br> | 1062 |
|      |      | CCC<br>Pro<br>350 |      |      |      |      |      | 1110 |
|      |      | ATC<br>Ile        |      |      |      |      |      | 1158 |
|      |      | GCA<br>Ala        |      |      |      |      |      | 1206 |

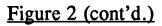
#### Figure 1 (cont'd.)

|      |       |       |      |      | AAC<br>Asn        |     |       |    |      |      |     |      |      |     |  | 1254 |
|------|-------|-------|------|------|-------------------|-----|-------|----|------|------|-----|------|------|-----|--|------|
|      |       |       |      |      | ACA<br>Thr        |     |       |    |      |      |     |      |      | -   |  | 1302 |
|      |       |       |      |      | ACC<br>Thr<br>430 |     |       |    |      |      |     |      |      |     |  | 1350 |
|      |       |       |      |      | CCT<br>Pro        |     |       |    |      |      |     |      |      |     |  | 1398 |
|      |       |       |      |      | GTG<br>Val        |     |       |    |      |      |     |      |      |     |  | 1446 |
|      |       |       |      |      | AAT<br>Asn        |     |       |    |      |      |     |      |      |     |  | 1494 |
|      |       |       |      |      | GTG<br>Val        |     |       |    |      |      |     |      |      |     |  | 1542 |
|      |       |       |      |      | GTG<br>Val<br>510 |     |       |    |      |      |     |      |      |     |  | 1590 |
|      |       |       |      |      | GAA<br>Glu        |     |       |    |      |      |     | TGA: | rggg | GCT |  | 1636 |
| GGGG | CTTTC | GGG ( | CTTG | CCTG | CC AC             | CAG | rgat( | TC | CCAC | CCTG | TTC | A    |      |     |  | 1680 |

| AAAG                  | AAGP | AGA ( | CCT | CCTAC | SA AZ | AAGT <i>I</i> | LAAA! | Thi |  | 1 G13 | A GAG | 54  |
|-----------------------|------|-------|-----|-------|-------|---------------|-------|-----|--|-------|-------|-----|
| CCC ?                 |      |       |     |       |       |               |       |     |  |       |       | 102 |
| CGC Arg 5             |      |       |     |       |       |               |       |     |  |       |       | 150 |
| GTT Z                 |      |       |     |       |       |               |       |     |  |       |       | 198 |
| GCT (                 |      |       |     |       |       |               |       |     |  |       |       | 246 |
| ATG Met               |      |       |     |       |       |               |       |     |  |       |       | 294 |
| ATG /                 |      |       |     |       |       |               |       |     |  |       |       | 342 |
| GTC :<br>Val '<br>105 |      |       |     |       |       |               |       |     |  |       |       | 390 |
| TGC (                 |      |       |     |       | -     |               |       |     |  |       |       | 438 |
| ATT (                 |      |       |     |       |       |               |       |     |  |       |       | 486 |
| GAA .                 |      |       |     |       |       |               |       |     |  |       |       | 534 |
| GCC Ala               |      |       |     |       |       |               |       |     |  |       |       | 582 |
| GCC<br>Ala<br>185     |      |       |     |       |       |               |       |     |  |       |       | 630 |

#### Figure 2 (cont'd.)

|      |      | AAC<br>Asn            |      |      |      |      |      | 678  |
|------|------|-----------------------|------|------|------|------|------|------|
|      |      | GAG<br>Glu            |      |      |      |      |      | 726  |
| <br> | <br> | GTG<br>Val            |      |      |      |      |      | 774  |
|      |      | GGT<br>Gly            |      |      |      |      |      | 822  |
|      |      | TTC<br>Phe<br>270     |      |      |      |      |      | 870  |
|      |      | ATG<br>Met            |      |      |      |      |      | 918  |
|      |      | GTG<br>Val            |      |      |      |      |      | 966  |
|      |      | ACC<br>Thr            |      |      |      |      |      | 1014 |
|      |      | CCA<br>Pro            |      |      |      |      |      | 1062 |
| <br> | <br> | <br>GGA<br>Gly<br>350 | <br> | <br> | <br> | <br> | <br> | 1110 |
|      |      | TCT<br>Ser            |      |      |      |      |      | 1158 |
|      |      | GTG<br>Val            |      |      |      |      |      | 1206 |
|      |      | AAC<br>Asn            |      |      |      |      |      | 1254 |



|                |      |      |     |      |       |       |       | GAA<br>Glu<br>420 |     |      |  | 1302 |
|----------------|------|------|-----|------|-------|-------|-------|-------------------|-----|------|--|------|
| <br>           | <br> | <br> |     |      |       |       | _     | GCC<br>Ala        |     |      |  | 1350 |
| <br>           | <br> | <br> |     |      |       |       |       | GTC<br>Val        |     |      |  | 1398 |
|                |      |      |     |      |       |       |       | ATC<br>Ile        |     |      |  | 1446 |
|                |      |      |     |      |       |       |       | GTA<br>Val        |     |      |  | 1494 |
| <br>           | <br> | <br> |     |      |       |       |       | CAT<br>His<br>500 |     | <br> |  | 1542 |
|                |      |      |     |      |       |       |       | GAG<br>Glu        |     |      |  | 1590 |
|                |      |      |     |      |       |       |       | ACT<br>Thr        |     |      |  | 1638 |
| <br>AGT<br>Ser | -    |      | TAG | ACTA | ACA : | )AAA1 | GAAA( | CA C              | TTT |      |  | 1680 |

| GAT. | AGTG | CTG 1 | AAGA | GGAG | GG G( | CGTT | CCA | G AC | Met |  |  | ı Gly             | GCC<br>Ala | 54  |
|------|------|-------|------|------|-------|------|-----|------|-----|--|--|-------------------|------------|-----|
|      |      |       |      |      |       |      |     |      |     |  |  | CAT<br>His        |            | 102 |
|      |      |       |      |      |       |      |     |      |     |  |  | TGT<br>Cys        |            | 150 |
|      |      |       |      |      |       |      |     |      |     |  |  | GTC<br>Val        |            | 198 |
|      |      |       |      |      |       |      |     |      |     |  |  | ATC<br>Ile<br>70  |            | 246 |
|      |      |       |      |      |       |      |     |      |     |  |  | ATG<br>Met        |            | 294 |
|      |      |       |      |      |       |      |     |      |     |  |  | ATC<br>Ile        |            | 342 |
|      |      |       |      |      |       |      |     |      |     |  |  | ACG<br>Thr        |            | 390 |
|      |      |       |      |      |       |      |     |      |     |  |  | CTG<br>Leu        |            | 438 |
|      |      |       |      |      |       |      |     |      |     |  |  | AAG<br>Lys<br>150 |            | 486 |
|      |      |       |      |      |       |      |     |      |     |  |  | GAT<br>Asp        |            | 534 |
|      |      |       |      |      |       |      |     |      |     |  |  | CAA<br>Gln        |            | 582 |
|      |      |       |      |      |       |      |     |      |     |  |  | GCA<br>Ala        |            | 630 |

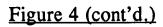
#### Figure 3 (cont'd.)

|      |            |      |             |     | GCC<br>Ala |             |      |      |     |      |             |       |     |     |       | 678  |
|------|------------|------|-------------|-----|------------|-------------|------|------|-----|------|-------------|-------|-----|-----|-------|------|
| 200  |            |      |             |     | 205        |             |      |      |     | 210  |             |       |     |     | 215   |      |
|      |            |      |             | Thr | GAG<br>Glu |             |      |      | Glu |      |             | -     |     | Ile |       | 726  |
|      |            | ama. | <b>63.6</b> | 220 |            | 63.T        |      | 3.00 | 225 |      |             |       | ~~~ | 230 |       | 77.4 |
|      |            |      |             |     | AAG<br>Lys |             |      |      |     |      |             |       |     |     |       | 774  |
| ասա  | ጥጥር        | ልጥጥ  | CCT         | ጥጥጥ | GGC        | <b>አ</b> ሞሮ | CCT  | ATG  | ccc | AAC  | ልጥር         | CCA   | СУТ | CAG | GCC   | 822  |
|      |            |      |             |     | Gly        |             |      |      |     |      |             |       |     |     |       | 622  |
|      |            |      |             |     | TTC        |             |      |      |     |      |             |       |     |     |       | 870  |
| Lys  | Leu<br>265 | Met  | Val         | Asp | Phe        | Phe<br>270  | Asn  | Ile  | Leu | Asn  | Glu<br>275  | Ile   | Val | Met | Lys   |      |
|      |            |      |             |     | ATG        |             |      |      |     |      |             |       |     |     |       | 918  |
| 280  | vai        | TIE  | Met         | 11e | Met<br>285 | Trp         | Tyr  | ser  | Pro | 290  | GIY         | 116   | Ala | Cys | 295   |      |
|      |            |      |             |     | ATT<br>Ile |             |      |      |     |      |             |       |     |     |       | 966  |
| 116  | Сув        | Gry  | гур         | 300 | 116        | VIG         | 116  | гур  | 305 | neu  | Giu         | Vai   | Val | 310 | ALG   |      |
|      |            |      |             |     | ATG<br>Met |             |      |      |     |      |             |       |     |     |       | 1014 |
| GIII | Leu        | O1,  | 315         | -1- | nec        | <b>va</b> 1 |      | 320  | 110 | 110  | O17         | Deu   | 325 | 116 |       |      |
|      |            |      |             |     | CCC<br>Pro |             |      |      |     |      |             |       |     |     |       | 1062 |
| Oly  | or,        | 330  |             | Deu | 110        | Deu         | 335  | -1-  | 1   |      | <b>V</b> 44 | 340   | 9   | 2,0 | 11011 |      |
|      |            |      |             |     | GCT<br>Ala |             |      |      |     |      |             |       |     |     |       | 1110 |
|      | 345        |      |             |     |            | 350         |      | •    |     |      | 355         |       |     |     |       |      |
|      |            |      |             |     | GCT<br>Ala |             |      |      |     |      |             |       |     |     |       | 1158 |
| 360  | 1111       | nia  | Sel         | 561 | 365        | GIY         | 1111 | Deu  | FIG | 370  | 1111        | rne   | nry | Cys | 375   |      |
|      |            |      |             |     | ATT<br>Ile |             |      |      |     |      |             |       |     |     |       | 1206 |
| GIU  | GIU        | noil | Leu         | 380 | 116        | vaħ         | пåв  | nry  | 385 | THE  | rrd         | FIIE  | val | 390 | FLU   |      |
|      |            |      |             |     | AAC<br>Asn |             |      |      |     |      |             |       |     |     |       | 1254 |
| 441  | OLY        | urd  | 395         | 116 | non        | ne c        | uah  | 400  |     | 1114 | Leu         | - 7 - | 405 | u   | 741   |      |

#### Figure 3 (cont'd.)

| GCC GCC A<br>Ala Ala I<br>4     |        |   | Gln M |         |       |      |     |      |      |       |   | 1302 |
|---------------------------------|--------|---|-------|---------|-------|------|-----|------|------|-------|---|------|
| CAG ATT G<br>Gln Ile V<br>425   |        |   |       |         |       |      |     |      |      |       |   | 1350 |
| GCC AGT A<br>Ala Ser I<br>440   |        |   |       |         | Thr   |      |     |      |      |       |   | 1398 |
| GCC GTG G                       |        |   |       |         |       |      |     |      |      |       |   | 1446 |
| TGG CTG C                       |        |   |       |         |       |      |     |      |      |       |   | 1494 |
| TTT GGG GG<br>Phe Gly A         |        |   | Tyr H |         |       |      |     |      |      |       |   | 1542 |
| ATT GAC TO<br>Ile Asp So<br>505 |        |   |       |         |       |      |     |      |      |       |   | 1590 |
| CAA TCC A<br>Gln Ser I<br>520   |        |   |       |         | His   |      |     |      |      |       |   | 1638 |
| CAA TGT G                       |        |   |       |         |       |      |     |      |      |       |   | 1686 |
| GTA ACT C                       |        |   |       |         |       |      |     |      |      |       |   | 1734 |
| GAA CCT TO                      |        |   |       | FAAGGAT | ATG A | GTCI | CAG | CA A | ATTC | [TGA] | A | 1785 |
| TAAACTCCC                       | C AGCG | r |       |         |       |      |     |      |      |       |   | 1800 |

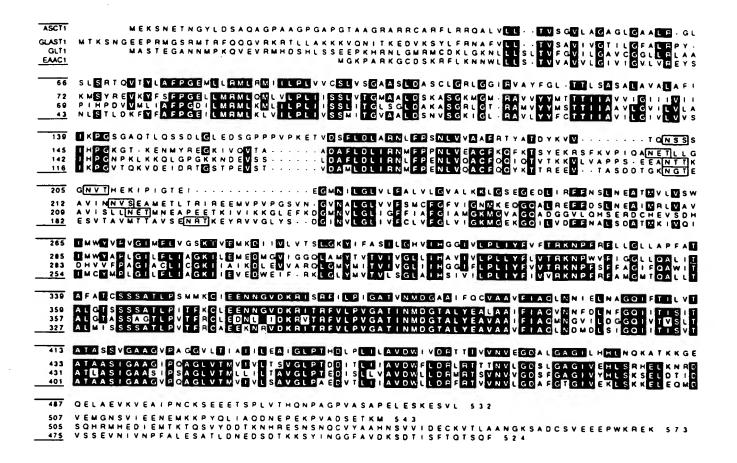
| ATAGCGGCGA CAGC |                |               | A GGA TGC CCG AG<br>s Gly Cys Pro Se<br>10 |  |
|-----------------|----------------|---------------|--|--|
|                 | Lys Asn Asn Tr |               | TCC ACC GTG GCC<br>Ser Thr Val Ala<br>25   |  |
|                 |                |               | CGA GAA CAC AGC<br>Arg Glu His Ser<br>40   |  |
|                 |                |               | CCT GGA GAA ATT<br>Pro Gly Glu Ile         |  |
|                 |                |               | ATT ATA TCC AGC<br>Ile Ile Ser Ser<br>75   |  |
|                 |                |               | TCC GGA AAA ATT<br>Ser Gly Lys Ile<br>90   |  |
|                 |                | e Cys Thr Thr | CTC ATT GCT GTT<br>Leu Ile Ala Val<br>105  |  |
|                 |                |               | GGT GTC ACC CAG<br>Gly Val Thr Gln<br>120  |  |
|                 |                |               | GAA GTC AGT ACG<br>Glu Val Ser Thr         |  |
|                 |                |               | CCT GAG AAT CTT<br>Pro Glu Asn Leu<br>155  |  |
|                 |                |               | GAA GAA GTG AAG<br>Glu Glu Val Lys<br>170  |  |
|                 |                | t Thr Glu Glu | TCC TTC ACA GCT<br>Ser Phe Thr Ala<br>185  |  |
|                 |                |               | GAA TAC AAA ATT<br>Glu Tyr Lys Ile<br>200  |  |

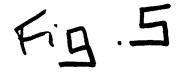


| 000     | 3 ma       | m> m       | max     | 0 N M      | 000        |            |      | c.m.c.     | ama           |     | mma        | » mm | ama        |            | ma.a | 675  |
|---------|------------|------------|---------|------------|------------|------------|------|------------|---------------|-----|------------|------|------------|------------|------|------|
| Gly     |            |            |         |            | GGC        |            |      |            |               |     |            |      |            |            |      | 675  |
| 205     |            |            |         |            | 210        |            |      |            |               | 215 |            |      |            |            | 220  |      |
|         |            |            |         |            | GTC        |            |      |            |               |     |            |      |            |            |      | 723  |
| Leu     | Val        | Phe        | Gly     | Leu<br>225 | Val        | Ile        | Gly  | Lys        | Met<br>230    | Gly | Glu        | Lys  | Gly        | Gln<br>235 | Ile  |      |
|         |            |            |         |            |            |            |      |            | 230           |     |            |      |            | 233        |      |      |
|         |            |            |         |            | AAT        |            |      |            |               |     |            |      |            |            |      | 771  |
| Leu     | Val        | Asp        | Phe 240 | Phe        | Asn        | Ala        | Leu  | Ser<br>245 | Asp           | Ala | Thr        | Met  | Lys<br>250 | Ile        | Val  |      |
|         |            |            | 2.0     |            |            |            |      | 2.0        |               |     |            |      |            |            |      |      |
|         |            |            |         |            | TAT        |            |      |            |               |     |            |      |            |            |      | 819  |
| GIN     | 116        | 255        | Met     | Сув        | Tyr        | met        | 260  | Leu        | GIĀ           | Tie | Leu        | 265  | Leu        | тте        | Ala  |      |
|         |            |            |         |            |            |            |      |            |               |     |            |      |            |            |      | 0.4  |
|         |            |            |         |            | GTT<br>Val |            |      |            |               |     |            |      |            |            |      | 867  |
| 017     | 270        |            |         |            |            | 275        |      |            |               |     | 280        | •••  | 2,0        | Lou        | Cly  |      |
| C T T T | ma.c       | አመሮ        | ccc     | 202        | GTC        | OTTC.      | » Cm | 000        | <b>C</b> IDIT | CCN | እመረ        | CAC  | maa        | » mm       | CMN  | 915  |
|         |            |            |         |            | Val        |            |      |            |               |     |            |      |            |            |      | 913  |
| 285     | _          |            |         |            | 290        |            |      |            |               | 295 |            |      |            |            | 300  |      |
| АТТ     | CTC        | CCG        | СТС     | АТА        | TAT        | ттс        | ATA  | GTC        | GTA           | CGA | AAG        | AAC  | ССТ        | ттс        | CGA  | 963  |
|         |            |            |         |            | Tyr        |            |      |            |               |     |            |      |            |            |      | 700  |
|         |            |            |         | 305        |            |            |      |            | 310           |     |            |      |            | 315        |      |      |
| TTT     | GCC        | ATG        | GGA     | ATG        | GCC        | CAG        | GCT  | CTC        | CTG           | ACA | GCT        | CTC  | ATG        | ATC        | TCT  | 1011 |
| Phe     | Ala        | Met        | _       | Met        | Ala        | Gln        | Ala  |            | Leu           | Thr | Ala        | Leu  |            | Ile        | Ser  |      |
|         |            |            | 320     |            |            |            |      | 325        |               |     |            |      | 330        |            |      |      |
| TCC     | AGT        | TCA        | GCA     | ACA        | CTG        | CCT        | GTC  | ACC        | TTC           | CGC | TGT        | GCT  | GAA        | GAA        | AAT  | 1059 |
| Ser     | Ser        | Ser<br>335 | Ala     | Thr        | Leu        | Pro        |      | Thr        | Phe           | Arg | Cys        |      | Glu        | Glu        | Asn  |      |
|         |            | 333        |         |            |            |            | 340  |            |               | ,   |            | 345  |            |            |      |      |
|         |            |            |         |            | AGG        |            |      |            |               |     |            |      |            |            |      | 1107 |
| Asn     | Gln<br>350 | Val        | Asp     | Lys        | Arg        | 11e<br>355 | Thr  | Arg        | Phe           | Val | Leu<br>360 | Pro  | Val        | Gly        | Ala  |      |
|         | 330        |            |         |            |            | 300        |      |            |               |     | 300        |      |            |            |      |      |
|         |            |            |         |            | GGG        |            |      |            |               |     |            |      |            |            |      | 1155 |
| 365     | TTE        | Asn        | Met     | Asp        | Gly<br>370 | Thr        | Ala  | Leu        | Tyr           | 375 | Ala        | vai  | Ala        | Ala        | 380  |      |
|         |            |            |         |            |            |            |      |            |               |     |            |      |            |            |      |      |
|         |            |            |         |            | AAT        |            |      |            |               |     |            |      |            |            |      | 1203 |
| rne     | 116        | VIG        | GIII    | 385        | Asn        | vaħ        | neu  | vaħ        | 390           | GIY | 116        | GIÀ  | GIII       | 395        | TIE  |      |
|         |            |            |         |            |            |            |      |            |               |     |            |      |            |            |      | 1051 |
|         |            |            |         |            | GCC<br>Ala |            |      |            |               |     |            |      |            |            |      | 1251 |
|         |            |            | 400     |            |            |            |      | 405        |               |     | 1          |      | 410        | 1          |      |      |

#### Figure 4 (cont'd.)

|                   |      |      |       |      | GTG<br>Val        |      |       |      |       |      |     |     |     |     | 129     | 9         |
|-------------------|------|------|-------|------|-------------------|------|-------|------|-------|------|-----|-----|-----|-----|---------|-----------|
|                   |      |      |       |      | GTC<br>Val        |      |       |      |       |      |     |     |     |     | <br>134 | 17        |
|                   |      |      |       |      | ATG<br>Met<br>450 |      |       |      |       |      |     |     |     |     | 139     | )5        |
|                   |      |      |       |      | CTC<br>Leu        |      |       |      |       |      |     |     |     |     | <br>144 | 3         |
|                   |      |      |       |      | ATT<br>Ile        |      |       |      |       |      |     |     |     |     | <br>149 | 1         |
|                   |      |      |       |      | TCA<br>Ser        |      |       |      |       |      |     |     |     |     | 153     | 9         |
|                   |      |      |       |      | TCT<br>Ser        |      |       |      |       |      |     |     |     |     | 158     | <b>;7</b> |
| TTC<br>Phe<br>525 | TAGO | GCC  | CCT ( | GCT  | GCAG <i>i</i>     | AT G | ACTGO | GAAA | C AAC | GAAC | GAC | ATT | CGT | GAG | 164     | 10        |
| AGTO              | CATC | CA ! | AACAG | CGGC | T A               | AGGA | AAAG  | A GA | λA    |      |     |     |     |     | 167     | 4         |





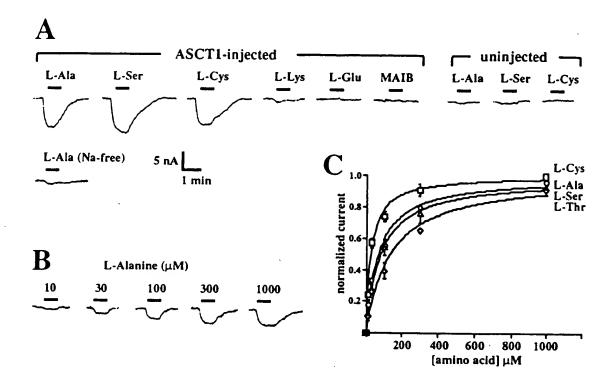
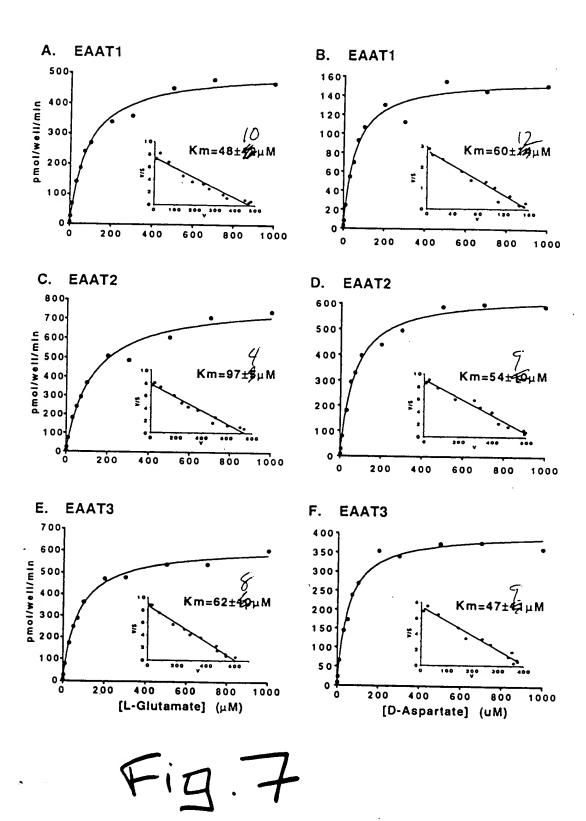
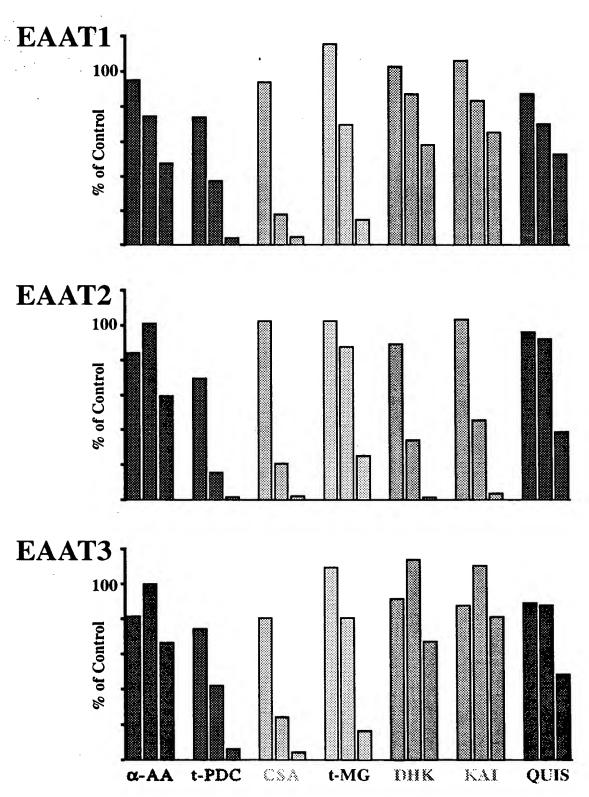


Fig. 6



## Pa. B

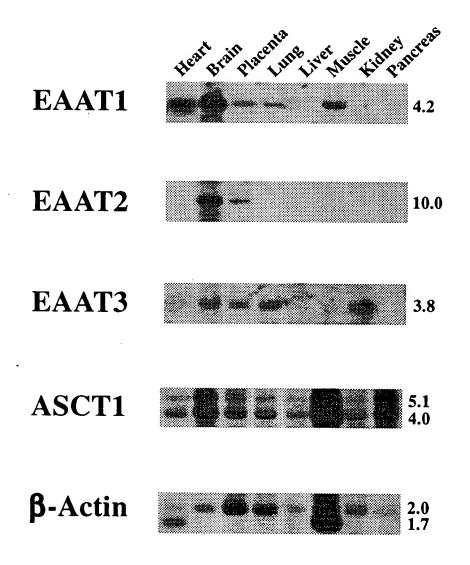
### Glutamate Transporter Pharmacology



1  $\mu M$  L-Glu with inhibitors at 3  $\mu M$ , 100  $\mu M$ , or 3 mM

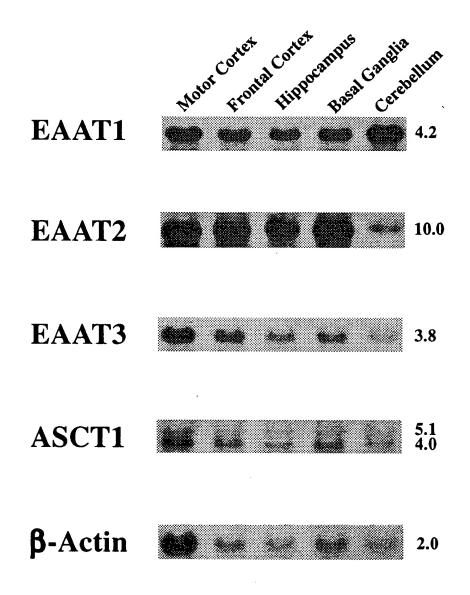
### F19.9

# Distribution of Transporter mRNAs in Human Tissues



### Fig. 10

## Distribution of Transporter mRNAs in Regions of the Human Brain



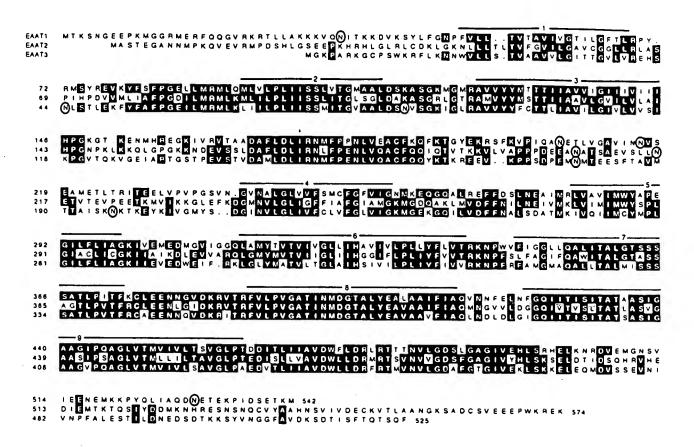


Fig. 11

A

| 100 μΜ |       |       | 1000 μΜ |       |       |                    |  |
|--------|-------|-------|---------|-------|-------|--------------------|--|
| L_Glu  | L_Asp | D-Glu | L-Ala   | L-Ser | L-Cys | (Na-free)<br>L-Glu |  |
| 100 nA |       |       |         |       |       |                    |  |

B.

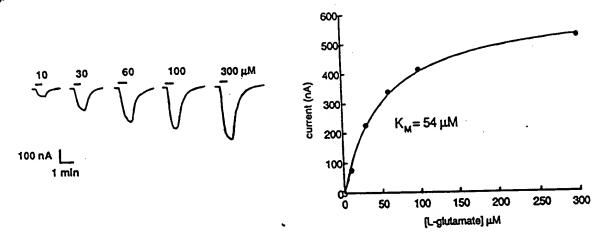


Fig. 12